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Effects of lidocaine, gabapentin, and dexmedetomidine on hemodynamic response during laryngoscopy and intubation

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Abstract

Aim: In this study, we aimed to compare the preventive effects of lidocaine, gabapentin and dexmedetomidine on hemodynamic response secondary to laryngoscopy and intubation.

Material and Methods: One hundred twenty ASA I-II patients, aged between 18-50 years who underwent elective tympanomastoidectomy under general anesthesia were enrolled in the study. Patients were randomly divided into 4 groups, each containing 30 patients. Groups 1, 3, and 4 were given placebo tablets orally 1 hour before the operation, Group 2 was given 1600 mg of gabapentin. Ten minutes before the operation, 1.5 mg/kg of 2 % lidocaine was applied to Group 1, 10 ml iv physiological serum was applied to Group 2, 1 mg/kg dexmedetomidine was applied to Group 3 and 10 ml iv physiological serum was applied to Group 4.

Results: Heart rates were significantly lower in Group 3 during induction, 3, 5. minutes after induction and in Group 2, 3, 5. minutes after induction when compared to other groups ($p<0.05$). OAP values in Groups 1 and 4 at 3 minutes after induction were significantly higher than basal values at 3 minutes ($p<0.05$).

Discussion: Dexmedetomidine and gabapentin applied before induction were found to be successful in the suppression of hemodynamic response secondary to intubation and in providing a stabilized hemodynamic status.

Keywords

Dexmedetomidine, Gabapentin, Hemodynamic Response, Intubation, Lidocaine

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Introduction

Laryngoscopy and tracheal intubation performed during general anesthesia have been known to produce adverse hemodynamic stress responses, such as tachycardia, systemic hypertension, and arrhythmia [1]. Adverse effects are more pronounced in patients with conditions such as coronary artery disease, myocardial infarction, or intracranial aneurysm. Certain medications such as beta-blockers, lignocaine, and opioids are used to mitigate the negative effects of laryngoscopy and intubation [2].

Gabapentinoids are second-generation anticonvulsants that are effective in the treatment of chronic neuropathic pain. Gabapentin binds to the α2δ subunit of voltage-gated Ca^{2+} channels that maintain increased release of pain transmission at nerve connections between primary afferent fibers and secondary common sensory nerves in chronic pain states. At the same time, it has been argued that its perioperative use effectively reduces the response to postoperative analgesia, preoperative anxiolytics, laryngoscopy, and intubation, while preventing postoperative chronic pain, postoperative nausea, vomiting, and delirium [3,4].

Lidocaine is a local anesthetic and is thought to effectively suppress the hemodynamic response to endotracheal intubation [5]. Dexmedetomidine is an imidazole derivative that binds with high selectivity to α2 receptors. These receptors are located in various structures such as blood vessels that regulate vasodilation, sympathetic terminals that inhibit the release of norepinephrine, the central nervous system that reduces both sedation and activity of the vagus, and the spinal cord that regulates analgesia [6].

This study was designed to compare the efficacy of lidocaine, gabapentin, and dexmedetomidine in suppressing the stress response induced by laryngoscopy and endotracheal intubation.

Material and Methods

The study was conducted after obtaining the written informed consent from the patients and the approval of the local ethics committee (06-2008/13). A total of 120 patients between the ages of 18 and 50 in the American Society of Anesthesiologists (ASA) I–II risk group who were planned to undergo elective tympanomastoidectomy were included in the study. This study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki revised in the year 2000.

The following patients were excluded from the study: those allergic to anesthetics or any other drugs, those with an alcohol or drug addiction, psychiatric and neurological disorders, asthma, hematologic disorders, hepatic and renal failure, cardiac disease, uncontrolled hypertension, hypovolemia or dehydration, or those found to be obese (body mass index over 30), pregnant or in ASA II, which were considered to cause difficulty in intubation or providing airway (a Cormack–Lehane and Mallampati score of III or IV).

One day before surgery, the patients were informed in detail and in an understandable way about the procedure to be performed and their written consent was obtained. The ASA and Mallampati classifications were determined through physical examination of the patients. No premedication was administered to them. The patients were randomly divided into four groups each with 30 subjects. Group 1 (lidocaine, n=30) cases: supplemented to 10 ml with an oral placebo tablet (sugar tablet) one hour before surgery and 1.5 mg/kg IV lidocaine (Aritmal®, Biosel, Istanbul) SF 10 minutes before surgery. Group 2 (gabapentin, n=30) cases: 1600 mg gabapentin orally (Neurontin®, Pfizer, Istanbul) one hour before surgery and 10 ml IV saline (SF) 10 minutes before surgery. In Group 3 (dexmedetomidine, n=30) cases: supplemented to 10 ml one hour before surgery with an oral placebo tablet and with 1 μg/kg IV dexmedetomidine (Precedex®, Abbott, USA) SF 10 minutes before surgery. Group 4 (control, n=30) cases: administered an oral placebo tablet one hour before surgery and 10 ml IV saline 10 minutes before surgery. The gabapentin and oral placebo tablets used in the study were administered by a nurse who had no affiliation with the study. Patients were routinely monitored with electrocardiogram (ECG), peripheral oxygen saturation (SpO2), and mean arterial pressure (MAP). After preoxygenation with a mask for 5 minutes with 6 l/min 100% O2, intravenous induction was performed with 1 μg/kg fentanyl (Fentanyl®, Abbott, USA), 2 mg/kg propofol (Propofol® 1%, Fresenius Kabi, Germany) or 0.1 mg/kg vecuronium bromide (Norcuron®, Organon, Netherlands). At 3 minutes after loss of verbal response and ciliary reflex, intubation was performed. Anesthesia was maintained with a gas flow of 3 l/min from 50% oxygen, 50% air, and one MAC sevoflurane (Sevorane, Abbott, UK) inhalation. To maintain muscle relaxation, an additional 0.02 mg/kg of vecuronium was administered as required. Cormack–Lehane classification was recorded for each patient.

HR, SpO2, and MAP values were recorded preoperatively, during induction, at 1, 3, 5, 10 and 15 minutes after induction, and every 30 minutes thereafter. After discontinuation of sevoflurane five minutes before the end of skin suture removal, and spontaneous breathing or muscle movement in the patient, neuromuscular blockade was antagonized with 0.02 mg/kg atropine (Atropine®, Biosel, Istanbul) and 0.06 mg/kg neostigmine (Neostigmine®, Adeka, Samsun). Patients were extubated when they had adequate spontaneous breathing. Anesthesia duration was determined as the time from IV induction drug administration to inhalant occlusion, and surgical duration was determined as the time from skin incision to the removal of the last skin suture. The duration of extubation was also measured and recorded. The duration of the Aldrete score of 8 was recorded.

Any side effects experienced by the patients were recorded. If hypotension (more than 30% decrease from the initial MBP value) or bradycardia (HR < 45 beats/min.) developed, the inhalant concentration was to be reduced by 50% and 250 ml of saline was to be rapidly administered. If these findings persisted, hypotension would be treated with 5–10 mg IV ephedrine (Efedrin®, Biosel, Istanbul) and by administering 0.5 mg IV atropine if bradycardia occurred. If HR and MAP exceeded 30% of the control value, the inhalant concentration would be increased by 50%. Any side effects (hypotension, nausea, vomiting, tremor, headache) within the first 10 minutes after surgery were recorded.

The SPSS (Statistical Package for Social Sciences) package program for Windows 13.0 was used for statistical analysis of the findings obtained in the study. The chi-square test was

used to compare categorical measurements. A one-way ANOVA test was used for statistical analysis. Any significantly altered parameters were then compared with Tukey's test as a post-hoc test. In the evaluation of hemodynamic parameters, group comparison was performed using a one-way ANOVA test. The results were within the 95% confidence interval and $p < 0.05$ was considered statistically significant. Data were expressed as mean ± standard deviation.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The demographic characteristics of the cases included in the study, their Cormack–Lehane (C-L) classification, and their Mallampati classification, duration of anesthesia, and surgical duration are shown in Table 1.

There was no statistically significant difference between the groups in terms of loss of response to verbal stimuli and duration of loss of eyelash reflex (Table 2).

When comparing the groups in terms of HR, HR values were found to be significantly lower at induction, immediately after intubation (3rd minute after induction), and at the 5th minute after induction in Group 3 compared to the other three groups.

Table 1. Demographic data (arithmetic mean ± standard deviation)

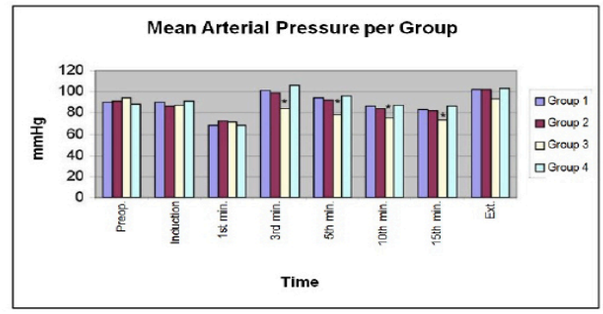
	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	Group 4 (n=30)	p
Age (years)	28.6±9.8	29.9±10.5	29.3±9.6	28.3±10.2	0.931
Sex (F/M)	19.11	15/15	15/15	18.12	0.640
Weight (kg)	73.1±10.5	67.5±12.0	67.9±10.5	68.9±10.2	0.178
ASA (I/II)	13/17	14/16	19.11	14/16	0.410
C–L (I/II)	22.8	17/13	20.10	22.8	0.482
Mallampati Classification (I/II)	15/15	13/17	13/17	11.19	0.787
Duration of anesthesia (min)	134.5±5.4	135.2±3.4	133.9±6.2	135.0±3.1	0.752
Duration of surgery (min)	123.7±5.4	121.8±3.2	122.1±5.8	122.2±3.1	0.360

F: Female, M: Male, ASA: American Society of Anesthesiologists Classification, C-L: Cormack–Lehane Classification

Table 2. Duration of loss of response to verbal stimuli, loss of eyelash reflex and recovery data (arithmetic mean ± standard deviation) for each group.

	Group 1	Group 2	Group 3	Group 4	p
Loss of response to verbal stimuli (sec)	32.4±5.7	31.0±7.3	32.0±9.0	30.9±5.6	0.802
Loss of eyelash reflex (sec)	36.6±5.9	34.8±7.5	34.6±9.4	36.0±5.8	0.459
Spontaneous breathing (sec)	231.8±83.2	226.0±84.8	202.7±93.9	293.5±88.2*	0.001
Extubation duration (sec)	333.5±74.5	355.3±54.8*	355.6±87.9	428.7±103.5*	0.001
Eye-opening duration (sec)	450.3±69.6	452.1±73.2	455.1±112.9	530.2±127.3*	0.007
Duration for Aldrete score of 8 (sec)	660.0±102.8	649.0±66.2	636.6±87.3	762.6±79.9*	0.000

*: $p < 0.05$, difference between groups originating from Group 4



Preop: pre-operation

Ext.: extubation

*: $p < 0.05$, significant difference between groups originating from Group 3.

Figure 1. Mean Arterial Pressure per Group

HR values immediately after intubation (3rd minute) and at the 5th minute after induction were significantly lower in Group 2 compared to Group 1 and Group 4. When the groups were compared in terms of mean arterial pressure (MAP), MAP values immediately after intubation (3rd minute after induction), and at the 5th, 10th, and 15th minutes after induction were significantly lower in Group 3 compared to the other three groups (Figure 1). When spontaneous breathing time, extubation time, eye-opening time, and Aldrete score of 8 were evaluated between groups, it was found that the recovery data for Group 4 was significantly longer than for all other groups (Table 2).

Discussion

The main problems resulting from the hemodynamic response to laryngoscopy and tracheal intubation are tachycardia and hypertension. The hemodynamic response to laryngoscopy and tracheal intubation is suppressed by various medications, such as narcotic analgesics, deep inhalation anesthetics, local anesthetics, adrenoreceptor blockers, and vasodilators.

When the groups were compared in this study, HR values during induction, at the 3rd and 5th minutes after induction, MAP at the 3rd, 5th, 10th, and 15th minutes after induction, in the dexmedetomidine group were significantly lower than those of the other three groups. It was also found that HR values were significantly lower in the gabapentin group at 3 and 5 minutes after induction compared with the lidocaine and placebo groups. Dexmedetomidine generated better outcomes than the other three groups in terms of hemodynamic response to intubation. Gabapentin neither suppressed nor induced a pressure response. The hemodynamic data of the lidocaine group did not differ from that of the placebo group.

Cardiovascular problems resulting from sympathetic and sympathoadrenal reflexes are common complications of intubation [7]. Mendonça et al. compared the effects of esmolol and lidocaine in preventing a hemodynamic response due to endotracheal intubation. In their study, 69 ASA I–II patients aged between 18 and 70 years were randomly divided into two groups. Esmolol was found to be safer and more effective in reducing the incidence of tachycardia and controlling heart rate after tracheal intubation compared with lidocaine [8]. In this present study, it was found that lidocaine does not adequately

suppress the hemodynamic response to laryngoscopy and intubation, similar to the findings of the cited study. In addition, Zou et al. [9] reported that 1 6and 1.5 mg/kg intravenous lidocaine as an adjunct to sufentanil for induction of general anesthesia slightly lowered blood pressure after endotracheal intubation, without side effects. However, it was emphasized that it was unable to suppress the increase in heart rate caused by endotracheal intubation.

Mahiswar et al. [10] compared two groups administered 0.5 µg/kg dexmedetomidine (Group D) and 2 µg/kg fentanyl (Group F) before induction to reduce hemodynamic response to tracheal intubation. Conducted with 100 patients, this study concluded that dexmedetomidine 0.5 µg/kg administered as a bolus is as effective as fentanyl in attenuating the hemodynamic response to tracheal intubation. Reddy et al. [11] showed that the use of a single dose of dexmedetomidine before induction of general anesthesia is an effective method of reducing hemodynamic response to tracheal intubation.

In their study, Gulabani et al. concluded that administration of 1 µg/kg dexmedetomidine 10 minutes before induction of anesthesia effectively reduced hemodynamic response to laryngoscopy and intubation. In addition, 1.5 mg/kg lignocaine administered three minutes before laryngoscopy and intubation was more effective than 0.5 µg/kg dexmedetomidine in reducing the increase in systolic and diastolic blood pressure three minutes and five minutes after endotracheal intubation [12]. In this present study, the hemodynamic data of the lidocaine group did not differ from that of the placebo group, but it was found that 1 µg/kg IV dexmedetomidine 10 minutes before surgery was an effective agent that can be used to prevent hemodynamic response to intubation.

Gupta et al. [13] compared dexmedetomidine and clonidine as adjuvants to low dose opioids in attenuation of hemodynamic response to intubation. They found that the rise in HR and MAP at laryngoscopy and intubation was less in clonidine group as compared to fentanyl group, and dexmedetomidine was able to attenuate this rise completely.

Parida et al. [14] found that oral gabapentin (800 mg) administered alone as premedication two hours before laryngoscopy and intubation did not cause a significant decrease in hemodynamic responses compared with intravenous fentanyl administered five minutes before induction of anesthesia. They also found that the administration of both drugs had no additional benefit over administration of IV fentanyl alone. For this reason, they indicated that it may not be possible to obtain a satisfactory outcome in response to tracheal intubation with the anesthetic regimen they followed using an oral dose of gabapentin. In their study on 100 patients with controlled hypertension, Bala et al. found that a single or double dose of 800 mg gabapentin was equally effective as premedication for laryngoscopy and tracheal intubation [15]. In this present study, gabapentin was found to suppress the tachycardic response to intubation well. In addition, it was found that it provides stable hemodynamics by not causing an increase in blood pressure in response to intubation.

Ninety minutes before surgery, Kapse et al. gave 5 µg/kg clonidine orally to 30 patients and 800 mg gabapentin orally to another 30 patients. They found that both drugs effectively reduced the hemodynamic response to direct laryngoscopy. They reported that they lowered blood pressure equally, while gabapentin induced greater postoperative sedation. In this present study, gabapentin was found to be effective at suppressing the tachycardic response [16]. Similarly, Sharma et al. reported that 900 mg gabapentin administered orally two hours before induction of anesthesia is an effective premedication agent that can be used to reduce the hemodynamic response to laryngoscopy and intubation [17]. In their study on 90 patients, Vijayan et al. [18] showed that 1 µg/kg dexmedetomidine administered 10 minutes before induction is a valuable assistant to the balanced anesthesia technique to maintain hemodynamic stability. Singhal et al. [19] reported that 200 µg/kg clonidine administered orally 90 minutes before anesthesia was more effective in reducing the hemodynamic response to laryngoscopy and intubation compared with orally administered gabapentin (900 mg). In their meta-analysis, Doleman et al. [20] demonstrated the beneficial effects of gabapentin in reducing the hemodynamic response to intubation. In this present study, gabapentin was more effective than lidocaine and placebo in suppressing the hemodynamic response to laryngoscopy and intubation.

It has been reported that administration of 0.6 µg/kg dexmedetomidine before induction of anesthesia can reduce the stress response during intubation and stabilize hemodynamics. In addition, it has been shown that the onset of spontaneous breathing and extubation time are prolonged in dexmedetomidine-treated groups compared with non-administered groups [21].

In this present study, dexmedetomidine was effective in suppressing the hemodynamic response, similar to the results reported by Ye et al. [22]. This present study also found that dexmedetomidine was superior to both the control group and the lidocaine and gabapentin groups in suppressing the hemodynamic response. In addition, recovery time and time to leave the operating room were found to be shorter in the groups given lidocaine, gabapentin, and dexmedetomidine compared to the placebo group.

Conclusion

In conclusion, gabapentin and dexmedetomidine was more effective than lidocaine and placebo in suppressing the hemodynamic response to laryngoscopy and intubation. Hemodynamic parameters were more stable in patients treated with gabapentin and dexmedetomidine compared to those treated with lidocaine and placebo. Administration of dexmedetomidine before induction in patients undergoing tympanomastoidectomy provided acceptable surgical conditions by reducing the heart rate and blood pressure to acceptable levels throughout surgery. Dexmedetomidine and gabapentin have therefore been found to be effective agents in preventing hemodynamic response to intubation.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with

the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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